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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,597	04/15/2004	Stephen J. Pandol	034044.021CIP1	7147

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EXAMINER	
PAGONAKIS, ANNA	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
11/13/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/824,597	PANDOL ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-57* is/are pending in the application.

4a) Of the above claim(s) *47-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 37-46 are currently under examination and the subject of this Office Action.

Applicant's amendment filed 9/25/2008 has been received and entered into the present application.

Claims 37-57 are currently pending. Accordingly claims 37, 40, 44 and 46 have been amended. Claims 47-57 are newly added.

Applicant's arguments, filed 9/25/2008 have been fully considered. Rejections not reiterated from the previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Withdrawal of Newly Added Claims: Election by Original Presentation

Applicant's amendment to add new claims 47-57 have been carefully considered in light of the subject matter that was elected and examined in the previous Office Action.

The MPEP states at 819:

"The general policy of the Office is not to permit the Applicant to shift to claiming another invention after the election is once made and action given to the elected subject matter."

Newly added claims, 47-57, are directed to a patentably distinct invention for the following reasons: originally filed claims 47-57 were directed to a therapeutically effective amount of rottlerin or derivative thereof, as elected by Applicant, whereas the newly amended claims are directed to the structural formula of claim 47. The structural formula of claim 47 does not encompass the chemical structure of rottlerin and as such, defines an independent and distinct invention as it is not accorded the

status of a "derivative of" rottlerin. Accordingly, the subject matter of newly added claims 47-57 is a patentably distinct invention.

Since Applicant has received an action on the merits for the originally presented invention directed to the administration of the elected compound for the treatment of cancer, this invention has been constructively elected by original presentation for prosecution on the merits. As a result, the amendment and inclusion of a new structural formula is withdrawn from consideration as being directed to a non-elected invention. Please see 37 CFR 1.142 (b) and MPEP 821.03. As stated in the MPEP at 818.02(a), "The claims originally presented and acted upon by the Office on the merits determine the invention elected by an Applicant in the application, and in any request for continued (RCE) which has been filed for the application. Subsequently presented claims to an invention other than that acted upon should be treated as provided in MPEP 821.03."

For these reasons, the inclusion of the new structural formula in newly added claims 47-57 is withdrawn from consideration pursuant to 37 CFR 1.142(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner

to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. (US 5,821,072) and Gschwendt (Biochem Biophys Res Commun, 1994) and Mouria (Int. J. Cancer, 98, 761-769, 2002).

Schwartz et al. teach an invention for enhancing therapy in a tumor bearing subject comprising administering to the subject an effective amount of a specific protein kinase C inhibitor capable of potentiating apoptosis in tumor cells during or prior to the treatment of an antitumor therapeutic agent (column 2, lines 56-61). The tumor can be a pancreatic cancer (column 3, line 14).

Gschwendt et al. teach of rottlerin as a novel protein kinase inhibitor which specifically inhibits PKC. Additionally it is taught that rottlerin can differentiate between PKC isozymes such as delta, epsilon, eta and zeta. The chemical structure of rottlerin might serve as a basis for the development of novel inhibitors with improved selectivity for distinct PKC isoenzyme such as PKC delta.

Mouria et al. teach that the effects of genistein was investigated on pancreatic carcinoma cells (abstract). Inhibitory effects of genistein on the development of metastatic lesions and the growth of the primary tumor in the same model of pancreatic cancer was observed (bridging pages 763-764). Genistein is also known to stimulate both apoptosis and caspase activation (page 765). Finally, the authors conclude that the genistein causes apoptosis in pancreatic cancer cells (page 766, column 2, paragraph 4).

One of ordinary skill in the art would have a reasonable expectation of success that rottlerin, a known PKC inhibitor would be effective against pancreatic cancer. Such success is expected since a protein kinase C inhibitor is known for the treatment of pancreatic cancer, Schwartz et al., and rottlerin is a known PKC inhibitor, Gschwendt et al. It would further be obvious to one of ordinary skill in the art to additionally administer genistein which is known for the treatment of pancreatic cancer. One of ordinary

skill in the art would have been motivated to combine the references since as combined would teach the invention as claimed.

Applicant's Remarks

Applicant alleges that merely because PKC inhibitor and other PKC inhibitors are known to potentiate apoptosis in tumor cells is not enough to make the leap to the assumption that rottlerin will likely be successful in treating pancreatic cancer. Further, Applicant alleges that this leap cannot be made because the review by Mackay et al teach that "both the activation and inhibition of PKC has been linked to the induction of apoptosis" (page 8 of the instant response). Finally, Applicant contends that the "duality of the PKC activation and inhibition" would not lead one of ordinary skill in the art to expect success until rottlerin was actually tested in pancreatic cancer models.

Response to Applicant's Arguments

Applicant's amendments and remarks have each been carefully considered in their entirety, but fail to be persuasive in establishing error in the propriety of the present rejection.

Examiner contends that Schwartz et al teach PKC is capable of potentiating apoptosis in *pancreatic cancer cells.* Schwartz et al specifically contemplate the use of PCK inhibitors in the treatment or potentiation of apoptosis in pancreatic cancer (see column 3, lines 11-16) and its used in combination with other therapeuctic agents (column 3, lines 17-22, pages 554-562) and columns 5-6 bridging paragraph. Applicant's cite Makay et al (Nature, Vo.l. 7, July 2007) that teaches that PKC activation or inhibition has been linked to the induction of apoptosis without specifying which cell types (or any cell types) activate PKC to induce apoptosis and which cell types inhibit PKC to induce apoptosis (page 55, column 1, paragraph 1 of Mackay et al). Further, the evidence provided is not drawn to any particular inhibitor, pancreatits, or pancreatic cancer since Applicant's reference fails to teach, in any

instance, the elected inhibitor of rottlerin has differential effects in different pancreatic tumor cells or different types of tumor cells. Finally, Applicants argue that PKC inhibitors both activate and inhibit apoptosis. This is not persuasive because this fact was known to the art and is not particular to the claimed PKC inhibitor, rottlerin. If the effect of PKC inhibitors is so cell and tumor specific as to be so unpredictable from one pancreatic tumor cell to another type of pancreatic tumor cell line, then Applicant's arguments/evidence is not commensurate in scope with their own claims because the claims encompass any type of pancreatic cancer or pancreatitis and applicants own specification is severely limited to a particular tumor cell line. Applicant's evidence is not directed to the claimed PKC inhibitor and the art specifically directs one skilled in the art to PKC inhibitors to potentiate apopotosis in pancreatic cancer (Schwartz et al). Finally, Applicants argue that the art is so unpredictable that success can not be ascertained unless the experiments have been performed. This is not persuasive because the statute does not require absolute prediction of success, only a reasonable expectation of success, and Schwartz et al provides that reasonable expectation of success.

Conclusion

No claim is found to be allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645